IMPACT ASSESSMENT OF PHARMACEUTICAL CARE INTERVENTION ON NEWLY DIAGNOSED DIABETES MELLITUS PATIENTS IN A TERTIARY CARE HOSPITAL OF A SUB METROPOLITAN CITY OF WESTERN NEPAL

by

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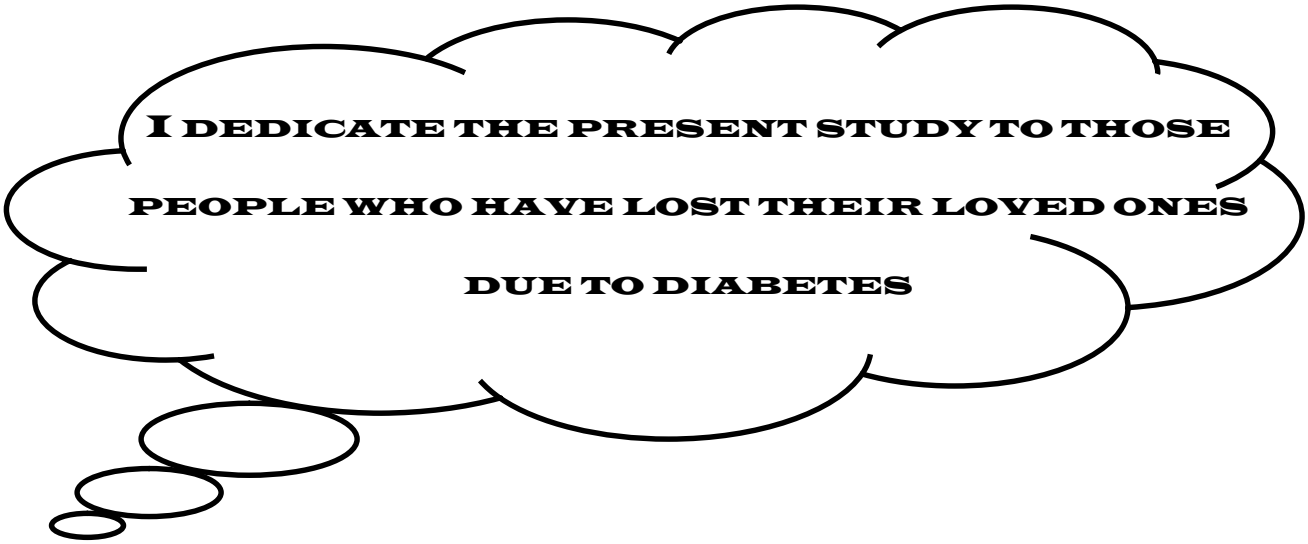
DEDICATION


I DEDICATE THE PRESENT STUDY TO THOSE
PEOPLE WHO HAVE LOST THEIR LOVED ONES
DUE TO DIABETES

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12M	Twelve month
3M	Three month
6M	Six month
9M	Nine month
ADA	American Diabetes Association
ADDQoL	Audit of Diabetes-Dependent Quality of Life
A-Score	Attitude score
AWIS	Average Weighted Impact Scores
BL	Baseline
BMI	Body Mass Index
BT	Backward Translator
CD	Cognitive Debriefing
CG	Control group
DAFNE	Dose Adjustment for Normal Eating
DBP	Diastolic Blood Pressure
DDP	Daily Dietary Plan
DHCs	Direct Healthcare Costs
DIMS	Diabetes Impact Measurement Scale
DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
DMC	Daily Medication Calendar
DPSQ	Diabetes Patient Satisfaction Questionnaire
F/U	Follow-up
FBG	Fasting Blood Glucose
FT	Forward Translator
GDM	Gestational Diabetes Mellitus
GQoL	General Quality of Life
HbA1c	Glycated Haemoglobin
HCPs	Health Care Professionals
HRQoL	Health-Related Quality of Life
IDDM	Insulin Dependent Diabetes Mellitus

IDF	International Diabetes Federation
IGT	Impaired Glucose Tolerance
IQR	Inter-quartile Range
KAP	Knowledge, Attitude and Practice
JNC	Joint National Committee
KAP-Scores	Knowledge, Attitude and Practice scores
K-Score	Knowledge score
LV	Linguistic Validation
MCC	Medication Counselling Centre
MODY	Maturity Onset Diabetes in Youth
NDA	Nepal Diabetes Association
NDI	Nurse Directed Intervention
NIDDM	Non Insulin Dependent Diabetes Mellitus
NKHC	Non-Ketotic Hyperosmolar Coma
NRs	Nepali Rupees
OBRA	Omnibus Reconciliation Act
OHAs	Oral Hypoglycaemic Agents
PC	Pharmaceutical care
PCI	Pharmaceutical Care Intervention
PCP	Pharmaceutical Care Program
PPBG	Post Prandial Blood Glucose
P-Score	Practice score
QoL	Quality of Life
RBG	Random Blood Glucose
SBP	Systolic Blood Pressure
SMBG	Self Monitoring Blood Glucose
SPSS	Statistical Package for Social Sciences
T1G	Test 1 group
T2G	Test 2 group
VLCD	Very Low Calorie Diet
WHO	World Health Organization
WIS	Weighted Impact Scores

PENILAIAN IMPAK PENJAGAAN FARMASEUTIKAL KE ATAS PESAKIT DIABETES MELLITUS YANG BARU DIDIAGNOS DI HOSPITAL PENJAGAAN TERTIAR DI BANDAR SUB METROPOLITAN NEPAL BARAT

ABSTRAK

Status sosioekonomi yang buruk dan kekurangan pengetahuan adalah kekangan utama yang perlu ditangani dalam pengurusan penyakit diabetes terutama dalam negara miskin. Oleh itu, satu kajian klinikal kawalan rawak telah dilaksanakan dalam 5 fasa dengan objektif untuk menilai impak intervensi penjagaan farmaseutikal ke atas tahap pengetahuan, sikap dan praktis (KAP), kualiti hidup berkaitan kesihatan (HRQoL), kepatuhan pengambilan ubat dan hasil akhir klinikal, kos penjagaan kesihatan langsung dan kepuasan pesakit diabetes mellitus yang baru didiagnos di hospital penjagaan tertiar. Satu sampel pesakit seramai 162 orang telah dipilih dari Julai 2010 sehingga Disember 2010 dan dirawak dengan cara 1:1:1 dalam tiga kumpulan selari: kumpulan kawalan (n= 54), kumpulan ujian 1 (n= 54) dan kumpulan ujian 2 (n= 54). Intervensi telah dijalankan menggunakan bahan dan alat pendidikan yang direka khas. Ujian Kruskal-Wallis, Mann-Whitney U, Friedman and Wilcoxon signed rank ($p \leq 0.05$) telah digunakan untuk mencari perbezaan manakala ujian korelasi Spearman ($p \leq 0.05$) telah digunakan untuk mencari hubungkait antara pembolehubah bersandar dan tak bersandar. Umur, pendapatan bulanan, jantina, pendidikan dan pekerjaan pesakit didapati berkaitan secara signifikan dengan skor pengetahuan, sikap dan praktis tentang diabetes dan pengurusannya. Skor HRQoL dan kepuasan didapati berkaitan secara negatif dengan umur mereka manakala umur, pendidikan dan pekerjaan pesakit adalah faktor peramal yang signifikan bagi kepatuhan pengambilan ubat. Pada tahap asas, pesakit mempunyai

pengetahuan dan praktis yang buruk tetapi secara relatif mempunyai sikap yang lebih baik tentang diabetes dan mereka menganggap kualiti hidup masa sekarang adalah buruk. Kepatuhan pesakit terhadap pengambilan ubat adalah baik tetapi kawalan glisemik adalah buruk. Hasil kajian juga menunjukkan kos penjagaan kesihatan langsung total adalah berpunca terutama daripada kos perubatan langsung dan pesakit kurang berpuas hati dengan penjagaan farmaseutikal pada tahap asas. Analisis ukuran berulangan menunjukkan penambahbaikan yang signifikan dalam skor pengetahuan, sikap, praktis dan KAP total, HRQoL, kepatuhan pengambilan ubat dan hasil akhir klinikal, kos penjagaan kesihatan langsung dan kepuasan pesakit pada setiap susulan ($p<0.001$) selepas intervensi. Berbanding dengan kumpulan kawalan, pesakit dalam kedua-dua kumpulan ujian menunjukkan tahap yang tinggi bagi pengetahuan [skor min ±sd (Kumpulan Kawalan (CG): 5.58±1.81; Kumpulan Ujian 1 (T1G): 13.18±1.57 dan Kumpulan Ujian 1 (T2G): 15.59±.72)], sikap positif [skor min ±sd (CG: 10.86±1.66; T1G: 13.04±1.37 dan T2G: 13.76±1.40)] dan praktis yang baik [skor min ±sd (CG: 6.86±1.08; T1G: 8.00±1.05 dan T2G: 9.47±.98)] pada susulan keempat, dan HRQoL mereka bertambah baik secara konsisten dengan peningkatan besar pada susulan keempat berbanding dengan tahap asas [skor median (CG: -3.16 berbanding -2.50; T1G: -2.56 berbanding -2.61 dan T2G: -2.26 berbanding -2.30)], dan oleh itu memperbaiki kualiti hidup umum mereka. Begitu juga, kepatuhan terhadap ubat [kepatuhan min ±sd (T1G: 96.53±1.04%; T2G: 97.68±.74% dan CG: 85.02±3.46%)] dan kawalan glisemik [median FBG, PPBG dan HbA1c (CG: 155, 186 dan 7.40%; T1G: 122, 148 dan 6.90%, dan T2G: 119, 145 dan 6.40%, masing-masing)] telah diperbaiki secara konsisten dalam kedua-dua kumpulan ujian dengan kepatuhan dan kawalan glisemik yang maksimum pada susulan keempat. Walau bagaimanapun, terdapat penurunan kos penjagaan

kesihatan langsung yang agak besar bagi pesakit dalam kedua-dua kumpulan ujian sepanjang susulan dengan penurunan yang besar pada susulan keempat [kos median dalam matawang Nepali (CG: 1851.50; T1G: 1020.00 dan T2G: 900.00); 1 USD = 73.38 Nepali rupees], dan mereka lebih berpuas hati dengan program penjagaan farmaseutikal dengan skor kepuasan yang lebih tinggi pada susulan keempat [skor median (CG: 47.74; T1G: 68 dan T2G: 73)]. Oleh itu intervensi penjagaan farmaseutikal menunjukkan hasil akhir yang positif bagi pesakit diabetes dari segi penambahbaikan pengetahuan, sikap dan praktis, HRQoL, kepatuhan terhadap pengambilan ubat dan hasil akhir klinikal, kepuasan dan pengurangan kos penjaagaan kesihatan langsung.

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ABSTRACT

Poor socioeconomic status and lack of knowledge regarding disease are the major hurdles to be addressed in management of the disease. Therefore, a randomised control trial (RCT) study was conducted in five phases with the objectives of evaluating the impact of pharmaceutical care intervention on knowledge, attitude and practice (KAP), health-related quality of life (HRQoL), medication adherence and clinical outcomes, direct healthcare costs and satisfaction of newly diagnosed diabetes mellitus patients in a tertiary care hospital. A sample size of 162 patients was selected over 6-months duration (from July 2010 to December 2010) and randomization was done by 1:1:1 in three parallel groups: control group (n= 54), test 1 group (n= 54) and Test 2 group (n= 54). Interventions were carried out with the used of specially designed educational materials and tools. Descriptive and inferential statistics were performed in each part of the study. Appropriate non-parametric tests such as Kruskal-Wallis, Mann-Whitney U, Friedman and Wilcoxon signed rank tests ($p \leq 0.05$) have been used to find out the differences while Spearman order correlation test ($p \leq 0.05$) was used to find out the association among different dependent and independent variables. Patients' age, monthly income, gender, education and occupation were significantly associated with their knowledge, attitude and practice scores about diabetes and its management. Patient's HRQoL and satisfaction scores were negatively associated with their age while age, education and occupation of the patients were the significant predictor of patient's medication

adherence. At baseline, patients had poor knowledge, practice but relatively better attitude regarding diabetes and they perceived their present quality of life as 'bad'. The medication adherence of the patients was considerable but they had poor glycaemic control. Total direct healthcare costs of patients were mainly attributable to direct medical costs, and patients were 'least satisfied' with pharmaceutical care at baseline. A repeated measure analysis showed significant improvement in knowledge, attitude, practice and KAP scores, HRQoL, medication adherence and clinical outcomes, direct healthcare costs and satisfaction of the patients in their each follow-up ($p<0.001$) following intervention. Compared to control group, patients of both test groups showed high degree of good knowledge [mean score±sd (CG: 5.58±1.81; T1G: 13.18±1.57 and T2G: 15.59±.72)], positive attitude [mean score±sd (CG: 10.86±1.66; T1G: 13.04±1.37 and T2G: 13.76±1.40)] and good practices [means score±sd (CG: 6.86±1.08; T1G: 8.00±1.05 and T2G: 9.47±.98)] at fourth follow-ups, and their HRQoL consistently improved with considerable improvement at the fourth follow-ups than baseline [median score (CG: -3.16 vs. -2.50; T1G: -2.56 vs. -2.61 and T2G: -2.26 vs. -2.30)], and hence improved their general quality of life. Similarly, medication adherence [mean adherence±sd (T1G: 96.53±1.04%; T2G: 97.68±.74% and CG: 85.02±3.46%)] and glycaemic control [median FBG, PPBG and HbA1c (CG: 155, 186 and 7.40%; T1G: 122, 148 and 6.90%, and T2G: 119, 145 and 6.40%, respectively)] were improved in both test groups consistently with maximum adherence and glycaemic control at fourth follow-ups. However, there were considerable reduction in total direct healthcare costs of patients in both test groups throughout with high reduction at the fourth follow-ups [median costs in Nepali rupees (CG: 1851.50; T1G: 1020.00 and T2G: 900.00); 1 USD = 73.38 Nepali rupees], and they were more satisfied with pharmaceutical care program

with greater satisfaction scores at fourth follow-ups [median score (CG: 47.74; T1G: 68 and T2G: 73)]. Thus, pharmaceutical care intervention showed positive outcomes for diabetes mellitus patients in terms of improving their knowledge, attitude and practice, HRQoL, medication adherence and clinical outcomes, satisfaction and minimizing their direct healthcare costs.

CHAPTER 1

GENERAL INTRODUCTION

1.1 INTRODUCTION

1.1.1 Background of diabetes mellitus

Diabetes has been recognised as a devastating and deadly disease for more than 2000 years. It was one of the first diseases described in an Egyptian manuscript in 1500 BC mentioning 'too great emptying of the urine'. Around the same time, Indian physicians also identified the disease and named it as '*madhumeha'* or '*honey urine'* and described 'a mysterious disease causing thirst, enormous urine output and wasting away of the body with flies and ants attracted to the urine of the people' (Das & Shah, 2011). The Greek Appollonius of Memphis first used the term 'diabetes' or 'to pass through' in 230 BC. The British surgeon John Rolle added the term 'mellitus' or 'from honey' to diabetes in the late 1700s and separated the condition named diabetes insipidus, which was also associated with frequent urination (MacCracken & Hoel, 1997).

Dr. Thomas Willis, a London-based physician, determined whether his patients had diabetes or not by sampling their urine in the 17th century. According to him, if urine had a sweet taste he would diagnose them with diabetes mellitus – "honeyed" diabetes. This method of monitoring blood sugar became very popular and remained unchanged until the 20th century. Different measures were tried in-between but effective treatment was not developed until the early part of the 20th century. Sushruta, Arataeus and Willis

were the early pioneers in the treatment of diabetes. Greek physicians used to prescribe exercise preferably on horseback to employ moderate friction and alleviate excess urination. There were different forms of remedy suggested for the therapy of diabetes including wine, overfeeding to compensate for loss of fluid weight, starvation diet, potato therapy and oat cure in olden days (Das & Shah, 2011). In 1913, scientist Allen, after three years of diabetes study, published a book named 'Studies Concerning Glycosuria and Diabetes'. This book encouraged scientists and doctors to develop therapies for diabetes patients.

In recent decades, the medical profession has advanced drastically and new technologies and medicines have been launched to treat heath-related problems, and to a certain extent this profession has taken up the challenges, but still there are many unresolved problems regarding patients' response towards therapy and better therapeutic outcomes resulting poor patients' satisfaction and high economic burden on them. These problems may be due to low patient involvement in their therapy, low level of their knowledge and awareness about their problem and sometimes poor healthcare facilities. Such problems become more challenging mainly in chronic disease conditions that require a long-term treatment strategy and special care and attention for the patient's benefit and a better therapeutic result.

Diabetes mellitus (DM) is a chronic disease condition with a rapidly increased prevalence and has become a serious healthcare challenge. At one time, this disease was considered as a problem of high-income countries (Balabanova et al., 2009), but now it is also growing rapidly even in low-income countries, mainly due to the change in lifestyle pattern, urbanisation and intake of high dietary fats (Moodley & Rambiritch,

2007). Increased incidence of diabetes has not only produced a clinical burden but also a social and economical burden (Kapur, 2007). Poor socioeconomic status and illiteracy leading to a lack of knowledge about the disease are the major hurdles in management of this disease (Mehta et al., 2006).

Diabetes mellitus is a heterogeneous disorder characterised by a varying degree of insulin resistance and insulin deficiency, which leads to disturbances in glucose homeostasis. It is commonly associated with prolonged ill-health and premature death. Chronic hyperglycaemia may lead to long-term complications that affect several organ systems and may lead to poor quality of life. These complications may cause disability and deformities among various organs. The mortality rate in patients with DM may be up to 4-5 times higher than in persons without the disease (Morgan et al., 2000). Diabetes is also the leading cause of stroke, renal failure, blindness and leg amputation in adults in developed countries (Centers for Disease Control and Prevention, 2011).

Patient knowledge of diabetes mellitus can assist in early detection of the disease and reduce the incidence of complications. The management of diabetes and its complications not only depends on drug therapy but also on physical exercise, controlled diet and other lifestyle modifications. Unless education is imparted and awareness is created among people, it is difficult to control the prevalence of diabetes. Diabetes education and awareness and improving motivation for self-care not only enhance care and reduce the burden of complication but also indirectly reduce the overall economic cost of diabetes (Kapur, 2001). Comprehensive patient education about diabetes and self-care skills is the cornerstone therapy for diabetes patients to attain tight glycaemic control (Asha et al., 2004).

1.2 Epidemiology of diabetes mellitus

1.2.1 Global scenario of diabetes mellitus

Diabetes is a serious condition not only for the individual, but also for society as a whole. Almost every country is under the burden of diabetes, which is considered a major public health problem. Diabetes is a metabolic syndrome, which if left untreated may lead to long-term life-threatening complications and premature death (Roglic et al., 2005).

The prevalence of diabetes has increased globally over the past two decades. Diabetes is accepted as the fourth- or fifth-leading cause of mortality among various diseases worldwide (International Diabetes Federation, 2011). Worldwide, several reports have been published on the prevalence of diabetes. In developed countries, the age group over 65 reflects the highest prevalence for the disease whereas in the developing world, greater prevalence occurs in the 45-64 years age-group (Wild et al., 2004). Diabetes currently affects 150 million people around the world and this number is expected to increase to 300 million by 2025 (King et al., 1998). The projected estimation reported by World Health Organization (WHO) and International Diabetes Federation (IDF) about the global prevalence of diabetes was 2.8% in 2000, and it would be increased to 4.4% in 2030 (Wild et al., 2004), and 366 million in 2011 and it is expected to be increased to 552 million by 2030 (International Diabetes Federation, 2011) respectively. The five countries with the highest diabetes prevalence in 2010 were Nauru (30.9%), United Arab Emirates (18.7%), Saudi Arabia (16.8%), Mauritius (16.2%) and Bahrain (15.4%) (Shaw et al., 2010). The United State of America (USA) was the

leading country among developed nations accounting for 26.8 million diabetic adults in 2010 and it is expected to increase to 36 millions by 2030 (Shaw et al., 2010).

Developing countries will be hit the hardest by the growing diabetes epidemic. Type 2 diabetes is more common in developing countries accounting for 90-95% of total cases (Mohan et al., 2007). An aging population, a shift towards a more sedentary lifestyle, increasing numbers of overweight and obese people, unhealthy diet and growing urbanisation are possible factors contributing to this alarming increase of diabetes prevalence (Amos et al., 1997; Zimmet et al., 2001). The incidence rate of diabetes is much higher in developing countries (170%) compared to developed countries (47%) (Zafar et al., 2011). Approximately 2-5% of adult populations located in industrialised countries are affected by diabetes (Atak & Arslan, 2005). The prevalence rate of diabetes is higher in the Asian nations. Approximately 50% of total global diabetes populations are located in Asian countries including Indian, China and Nepal. Among the top ten leading countries in terms of diabetes burden in the world, the top five are Asian countries, in which India (87 million) and China (62.6 million) are expected to be lead in terms of number of people with diabetes mellitus by 2030 (Cockram, 2000; Wild et al., 2004; Roglic et al., 2005; Mohan et al., 2007).

1.2.2 Prevalence of diabetes mellitus in Nepal

Nepal is located in between India and China. It is surrounded with hills and mountains and is nearly 500 miles long and 110 miles wide with a population of 28 million (Ministry of Health and Population, 2011). The country is divided into three geographical areas, the flat '*Terai planes'* in the south, the '*Central hills*' and the '*High*

Himalayas' in the north. This division has isolated the rural areas from the central areas and has hindered the development of transportation, communication and health facilities. In addition, about 90% of the population lives in rural areas (Singh, 2004).

The data suggest the percentage of diabetes dominancy in urban and rural areas is 25.9% and 3.1% respectively (Singh & Bhattarai, 2003). According to the Nepal Diabetes Association (NDA), approximately 15% of people more than 20-years old and 19% of people more than 40 years of age are affected with diabetes in urban areas (Bhattarai & Singh, 2007). As per the WHO estimation, more than 436,000 people are affected with diabetes in Nepal and the number is expected to increase to 1,328,000 by 2030 (Wild et al., 2004). The prevalence rate of type 2 diabetes mellitus and impaired fasting glucose have been reported as being about 9.0% and 19.2% respectively from one study conducted in a semi-urban population of Nepal (Ono et al., 2007). A recent study from Nepal also expected the prevalence of diabetes to be increased by 17% in 2020 (Dulal & Karki, 2009). The reasons behind the high prevalence of DM in Nepal are identified as low literacy, increased body weight due to intake of more fatty food, low physical activity and change in lifestyle (Upadhyay et al., 2008; Maskey et al., 2011).

1.3 Impact of diabetes mellitus and its complications

Diabetes affects persons of all ages, sexes and races. The disease reduces both a person's health-related quality of life (HRQoL) and life expectancy and imposes a large economic burden on their families, healthcare system and the nation. Diabetes is associated with serious long-term effects, which could have a huge impact on the quality of life of patients, especially when both micro-vascular and macro-vascular

complications are present. The risk factors for developing micro-vascular complications include duration of diabetes, glycaemic control and hypertension. The strongest risk factors for the development of macro-vascular complications include hypertension, hyperlipidaemia, smoking and albuminuria. Micro-vascular complications affect the small blood vessels and comprise of retinopathy, nephropathy and neuropathy. Macro-vascular complications encompass cerebrovascular disease, ischaemic heart disease and peripheral arterial disease (Marshall & Flyvbjerg, 2006). The risk for macro-vascular diseases tend to manifest in people with type 2 diabetes more than those diagnosed with type 1 diabetes, as hyperglycaemia contributes to the development of these complications. There is evidence that has proved the relationship between the degree of glycaemic control and the development of these complications (Klein & Klein, 1998; Stratton et al., 2000; American Diabetes Association, 2002a; Nordwall et al., 2009; Huang et al., 2011).

The incidence of mortality and disability due to diabetes is rising drastically all over the world. People with diabetes have an increased risk of mortality and morbidity compared with their non-diabetic counterparts. As pointed out by Mohan et al. in the 2009 the WHO report, there are about five times as many deaths indirectly attributable to diabetes (Mohan & Pradeepa, 2009). The death rate of men living with diabetes is 1.9 times and for women 2.6 times more than men and women without diabetes respectively (Lee et al., 2000). Premature mortality caused by diabetes results in an estimated 7 to 14 years of life lost compared to their non-diabetic counterparts (Narayan et al., 2003a; Manuel & Schultz, 2004; Andrade, 2010). The majority of the diabetes-related deaths are due to cardiovascular and cerebrovascular diseases and end-stage renal diseases

(Cusick et al., 2005). It is estimated that each year, approximately 3.8 million people die from diabetes-related complications worldwide (International Diabetes Federation, 2006).

In addition to the morbidity and mortality, diabetes exerts a heavy economic burden on the society. This burden is related to health-system costs incurred by society in managing the disease, indirect costs resulting from productivity losses due to patient disability and premature mortality, time spent by family members in seeking care of the patient and intangible costs (psychological pain to the family and loved ones). It was estimated that the total global cost to manage diabetes was USD 376 billion in 2010 and it is expected to increase to USD 490 billion in 2030. Globally, 12% of the health expenditure and USD 1330/person were anticipated to be spent on diabetes management during the year 2010. This expenditure may fluctuate by region, age, gender and country's income. This data shows the huge impact on a nation's economy. By looking at these results, there is a need for urgent measures for better understanding of the problem and novel strategies for prevention and treatment of the disease (Zhang et al., 2010).

1.4 Concept of pharmaceutical care vs. Medication therapeutic management

Diabetes mellitus is spreading like a slow poison all over the world and causing complications to the sufferer and affecting their quality of life and increasing the economic burden. An individual suffering from type 2 DM is responsible for himself/herself to a large extent since this disease is related to lifestyle and dietary habits. However, development of type 1 diabetes mellitus is related with autoimmune

destruction of the pancreatic β-cells, due to which there is absolute deficiency of insulin in the body. Quite often patients do not adhere with their pharmacological (medication) and non-pharmacological (lifestyle modification, dietary habits and importance of recommended physical activities) treatments that are required to achieve the desired metabolic control and thus minimise the emergence of micro- and macro-vascular complications. Such problems can be avoided by increasing medication-adherence and adopting appropriate non-pharmacological measures, in which the pharmacist can play an important role through a well-structured pharmaceutical care (PC) programme (Machado-Alba et al., 2011).

Pharmaceutical care involves identifying, resolving and preventing drug-related problems. It is well understood that the pharmacist deals with medicines all the time. Pharmaceutical care was the first integrated philosophy of pharmacy practice to combine the expertise of the pharmacist with influencing prescribing and evaluating the drug regimen on one side and medication counselling on the other side to improve the patients' therapeutic outcomes, including quality of life. The role and contribution of the pharmacist in the healthcare system to achieve therapeutic outcome was developed by Hepler and Strand in 1990 (Hepler & Strand, 1990). According to them, 'pharmaceutical care practice involves direct interaction between the pharmacist and the patient, with responsible provision of drug therapy in order to achieve definitive outcomes that improve a patient's quality of life and promote disease management'. These outcomes are: (1) cure of disease; (2) eradication or decrease of patients' symptomatology; (3) arresting or slowing of disease process; or (4) preventing a disease or symptomatology (Hepler & Strand, 1990). Later, the philosophy of Hepler and Strand was refined by

Cipolle et al. and they said that 'it is a patient-centred practice' (Cipolle et al., 2004). In both these definitions, the emphasis is on the patient and the pharmacist's responsibility to ensure good quality of care to the patient and to achieve better patient outcomes. The pharmacist's role has evolved over the twentieth century from mainly being product focused, preparing and dispensing drugs, into a more patient-orientated care provider, and pharmaceutical care may be the target for the pharmacy profession worldwide. Although, pharmaceutical care is delivered by many different healthcare professionals, the pharmacists can be regarded as specialists in this practice as their focus is on pharmacology and pharmacotherapy, important skills for providing pharmaceutical care.

Pharmaceutical care deals with the way people should receive and use medications and instructions for the use of medicines. It also deals with the responsibilities, medication surveillance, counselling and outcomes of care. Pharmaceutical care can be achieved through the performance of a team of healthcare professionals including the pharmacist, doctors, nurses and technicians. This facilitates good communication between the different members of the healthcare team and continuity of care (Hepler & Strand, 1990; Palaian et al., 2005; Hudson et al., 2007).

However, the concept of Medication therapy management (MTM) is a distinct service or group of services that optimizes drug therapy with the intent of improved therapeutic outcomes for individual patients. Medication therapy management includes five core components: a medication therapy review (MTR), personal medication record (PMR), medication-related action plan (MAP), intervention and/or referral, and documentation and follow-up. During the MTM session, the pharmacist identifies medication-related problem(s) and determines appropriate intervention(s) for resolution.

Often, the pharmacist collaborates with other health care professionals to resolve the identified problem(s) (American Pharmacist Association and National Association of Chain Drug Store Foundation, 2008).

1.5 Concept of pharmaceutical care in Nepal

It is evident that the pharmaceutical care concept is still in the theoretical stage in Nepal and the practice is non-existent. A thorough literature survey showed that studies are lacking in the area of pharmaceutical care in Nepal. In Nepal, pharmacists are still considered as 'medicine sellers' to the public and they are more product oriented rather than patient oriented (Khanal et al., 2010). Pharmacists are still not focused on their role in patient care in the present healthcare system of Nepal. A review by Bhandari and associates (2006) reported that pharmacists in the country were involved in providing drug information and research work in few Nepali hospitals (Bhandari et al., 2006) suggesting an emerging scope, although it is not substantial.

In the Nepalese context, pharmacists focus on the industrial sector or the teaching profession, and then open their ‘medicine shops’ after finishing their pharmacy education. Recently, in 2010, the pharmacy education system of Nepal put a step forward in pharmacy education and started the Pharm.D program in Kathmandu University with the objective of providing better knowledge and more recognition and opportunity to the pharmacy graduates in the healthcare sector (Bhuvan et al., 2011). By this program, the education system of Nepal has provided a clear understanding to the pharmacists on their responsibilities as a healthcare professional and their contribution as a pharmacist in patient care.

The present study also focused on the contribution of the pharmacist in patient care through the pharmaceutical care program. This study may circulate the clear concept of pharmaceutical care among the Nepali pharmacists and their role in patient care so that they become more patient-focused at the hospital and community level.

1.6 Pharmaceutical care and its importance in diabetes mellitus management

The need for intensive diabetes mellitus management is the subject of discussion and debate, and it is clear that intervention programs to improve diabetes care and outcomes are important (Gæde et al., 2003; Krass et al., 2007; Wubben & Vivian, 2008). People with diabetes stay in the hospital much longer than the non-diabetic subjects and therefore it is a major concern for the healthcare system. The healthcare system may adopt certain approaches to minimise the patient stay in the hospital by improving their symptoms. It has been reported that the frequency of hospitalisation of diabetes patients are 1.5 times more and on an average 2.8 days longer than their non-diabetic counterparts (Koproski et al., 1997; Puig et al., 2007).

The pharmacist's role through pharmaceutical care has come up with some definite outcomes in the form of improved clinical outcomes (significant glycaemic control), improved patient satisfaction, improved cost management and reduced hospital stay (Singhal et al., 2002; Davis et al., 2005; Scott et al., 2006; Krass et al., 2007; Wubben & Vivian, 2008; Al Mazroui et al., 2009; Monte et al., 2009; Venkatesan et al., 2012). Pharmacists are easily accessible to patients in comparison with other healthcare professionals and therefore can provide better healthcare services to people with diabetes. Diabetes patients who received monitoring by the pharmacist through the

pharmaceutical care program reduced glycated haemoglobin (HbA1c) level by an average 1.9% in a six month period (Rothman et al., 2003). Similarly, people with diabetes experience greater satisfaction with their care when they received proper diabetes education, proper medication counselling and instruction on diet and exercise from their pharmacists (Singhal et al., 2002; Cranor et al., 2003; Zanetti et al., 2007; Sriram et al., 2011). A study reported that diabetic patients are able to reduce their HbA1c level to 7% or below and decrease their unscheduled clinical visits if they are provided proper physician supervision and systematic monitoring by the pharmacist (Irons et al., 2002). Diabetes carries a huge medical cost for the patient and their family members and decreases the productivity rate. Studies from different countries have stated that a reduction in medical cost and an increase in their productivity rate can be achieved by improving the patient's symptoms and reducing the risk rate through a structured pharmaceutical care program (Cranor et al., 2003; Garrett & Bluml, 2005).

1.7 Problem statement

Diabetes is an emerging health problem in Nepal. The number of people with diabetes is increasing day by day. It is difficult to estimate exact number of diabetic patients due to a lack of proper research and documentation in Nepal. Moreover, many diabetes patients are not aware of their problem due to lack of knowledge and awareness (Mehta et al., 2006; Upadhyay et al., 2008). They are also not getting effective and appropriate treatment and advice due to lack of proper healthcare facilities. The second important aspect is the dietary habit, which is unique in Nepal and they still have the old traditional concept. Lack of proper knowledge about the disease and poor dietary education has resulted in late detection of the disease by the patients, thus this has been a burning

problem. Therefore, looking at these aspects, the study has concluded the following problems:

Past evidence suggests a lack of knowledge and awareness about diabetes among the Nepali diabetic population and unavailability of systematic valid plans to cope with such problems. Similarly, there has been a dearth of data and research to assess the health-related quality of life (HRQoL) of diabetes patients and no research has been done to date in Nepal to quantify HRQoL due to lack of a valid instrument to measure it in the native language. In addition, there is no systematic approach in Nepal to increase patient adherence to their medication, resulting in poor glycaemic control in diabetes patients. Furthermore, to the best of my knowledge, there has been no focus on direct health-care costs (direct medical and non-medical cost) from patients prospective and there is a scarcity of valid research and data related to it in the country as well.

Added to the above issues, information is lacking to establish the association between provided patient-care and patient satisfaction in diabetes management in the Nepali healthcare system. Moreover, pharmacist involvement in patient care is still not recognised in the Nepali healthcare system. In addition, the low literacy rate (age group 15+years, total literacy rate (%) 2008/09 was 56%) in the country (Ministry of Education, 2010) still raises concerns over patient's knowledge and acceptance of the PC concept. Although, the existing scarcity of data, a quick reflection over the health care situation and health seeking behaviours of the layman, raises much concern over the *'health concern'* among the citizens. Since diabetes is a chronic condition and may not present much of its symptoms at the initial stages one might have a poor *'health concern'* over the condition especially in a country where the vast majority of the

population is illiterate. In addition, one study established a relationship between economic condition, educational status and health-seeking behaviour of Nepali citizens (Subba, 2004). These entire observations make the necessity for need of in-depth study in relevant domains of diabetes research.

1.8 Rationale of the study and its importance

The pharmaceutical care concept and the role of the pharmacist in patient care is mainly popular in developed countries and several studies have been done in related areas (Clifford et al., 2002; Strand et al., 2004; Clifford et al., 2005; Davis et al., 2005; Al Mazroui et al., 2009; Correr et al., 2009; Neto et al., 2011). The total number pharmacists registered with Nepal Pharmacy Council till year 2010 were 1690 among 28 million population of the country, with the pharmacist-to-public ration of 1:16,568 (Nepal Pharmacy Council, 2010). But the pharmacist involvement in patient care is still not well recognized in developing countries like Nepal where the resources are limited and pharmacist are still recognized as mere *'drug seller'* (Palaian et al., 2005; Khanal et al., 2010). No research has been done to date that has focused on the pharmacist's role in patient care through a pharmaceutical care concept in healthcare services in Nepal. Due to limited resources and increasing population, the health-related problems like cardiovascular diseases, hypertension and diabetes have increased tremendously leading to long-standing complications and more mortality and morbidity. The reasons may be linked to low literacy, low knowledge and poor awareness about the disease condition in patients. Lifestyle changes, obesity, poor dietary habits (intake of more fatty food) and low physical activity are making these problems more aggressive and longer standing (Mehta et al., 2006; Upadhyay et al., 2008; Maskey et al., 2011).

Poor healthcare facilities combined with low knowledge and awareness in patients causes more patient's non-adherence to their medications leading to poor therapeutic outcomes (Whitley et al., 2006; Al-Qazaz et al., 2011) and requiring more hospital services. Together, this produces more economic burden on patients and their family members. Such problems become more complex in chronic disease conditions like diabetes where patients get overburdened with prescribed medication. Therefore, it requires a *bidirectional approach*. *First* and foremost, the diabetes educational program about the ways to prevent the disease should be organised on a large scale. *Secondly*, the diabetes patients should get proper treatment, counselling and advice as per their need. Early detection of DM can be helpful in managing the disease by exercise and controlled diet, which directly affects the patient's economic burden. Education and counselling would be helpful for the patient to maintain their blood glucose level, which directly affects the patient's quality of life. Very little work has been done in Nepal so far in this regard.

Therefore, by conducting this study, we will understand better about diabetes patients' knowledge and awareness of their disease and its effect on their attitude and practice. It also provides insight on the impact of diabetes on patient's health-related quality of life, medication adherence and clinical outcomes with emphasis of direct healthcare costs and satisfaction level of patients.

1.9 Contributions of the study findings

It was anticipated to have considerable contributions during beginning of the study. Those anticipated outcomes of the study during initiation were helpful to establish the importance of the pharmaceutical care concept in the healthcare system of Nepal where previously no studies have addressed this concept. It was also anticipated that the present study would be beneficial for the diabetes patients to improve their knowledge and awareness, which will help them to improve their attitude and practice and hence nourish their quality of life. The study will also provide a valid method to improve therapeutic outcome and decrease economic burden. This study might also convey the message to other healthcare professionals that the pharmacist is also an important member of the healthcare team and can play a major role in patient care.

In addition, this study was expected to contribute to a better understanding of future pharmacists about their role and place in the healthcare system and it may divert their thinking to become more patient oriented. This study is an attempt to sensitise the government and provide validated information to government officers and policy makers so that they would have a better idea about the pharmacist's place in the healthcare system and their role in patient care. The findings could also set up a good platform for future researchers and provide a well-established module and primary data for further research on a large scale. This study would develop the appropriate diabetic kit that can be used to educate the patients (especially uneducated patients) about their disease through live demonstrations for better understanding of the patients.

1.10 Study objectives

Keeping the vision of the research study shown in Figure 1.1, the overall research objectives are as follows:

1.10.1 General objective

The general objective of the research is to evaluate the impact of a pharmaceutical care intervention targeted at newly diagnosed diabetes mellitus patients in terms of knowledge, attitude, practice, health-related quality of life, medication adherence and clinical outcomes, direct healthcare costs and patient's satisfaction.

1.10.2 Specific objectives

The various specific objectives are as below:

1. To describe the demographic distribution of newly diagnosed diabetes mellitus population with respect to their age, gender, ethnicity, education level and occupation.

2. To evaluate the impact of pharmaceutical care intervention provided by the pharmacist in terms of knowledge, attitude and practice of patients about diabetes and its management.

3. To quantify the impact of pharmaceutical care intervention provided by pharmacist in terms of health-related quality of life outcomes of diabetes mellitus patients.

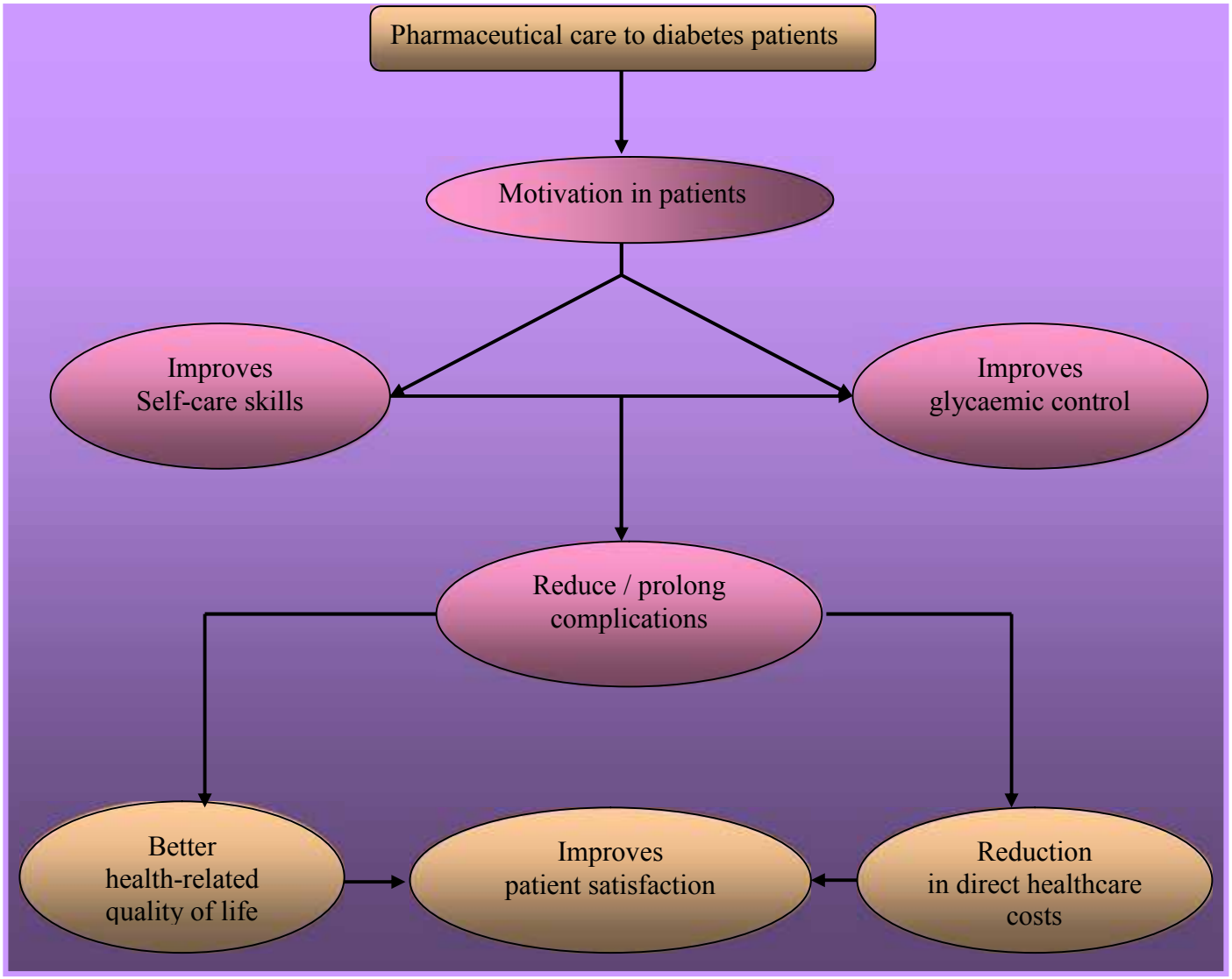

Figure 1.1 Vision of the overall research

4. To evaluate the impact of pharmaceutical care intervention provided by pharmacist in terms of medication adherence and clinical outcomes (i.e. glycaemia and blood pressure control), direct healthcare costs and satisfaction of diabetes mellitus patients.

1.11 Thesis overview

This thesis consists of seven chapters including this chapter (general introduction). **Chapter 2** is related to a literature review and the conceptual framework. This chapter gives brief information related to diabetes and its management followed by in-depth reviews of literature related to individual study objectives with a suitable definition of terms used wherever necessary. This chapter will be ending with the study's conceptual framework, research questions and hypothesis with a brief conclusion about significant gaps in diabetes care that need to be minimised with pharmacist intervention.

Chapter 3 will be basically discussing about general methodology used in present study. This chapter will highlight the detail explanation about the methodology used in present research study with description of different study tools and questionnaire formulation. This chapter also talks about how the intervention and reinforcement program was conducted for diabetes patients with a brief note on a pilot study conducted for methodology and tools' validation.

Chapter 4 is about the impact assessment of pharmaceutical care intervention on the knowledge, attitude and practice of newly diagnosed diabetes patients in tertiary care hospital. This chapter includes a detailed analysis of diabetes patients' knowledge, attitude and practice (KAP) about diabetes and its management with emphasis of the impact of the pharmacist-provided pharmaceutical care intervention on diabetes patients'

KAP. The chapter will be ending with detail discussion on study findings and conclusion.

Chapter 5 describes the impact assessment of pharmaceutical care intervention on health-related quality of life of newly diagnosed diabetes patients. This chapter provides a detailed description and analysis of diabetes impact on general and overall health-related quality of life of diabetes patients with emphasis on the impact of pharmaceutical care intervention on health-related quality of life of diabetes patients. The chapter ends with a discussion on the study findings and the conclusion.

Chapter 6 illustrates the impact assessment of pharmaceutical care intervention on medication adherence and clinical outcomes, direct healthcare costs and satisfaction of newly diagnosed diabetes patients. This chapter focuses initially on the pattern of medication adherence and clinical outcomes of diabetes patients, assessment of direct healthcare costs of patients and their satisfaction with an emphasis on the pharmacist intervention on these outcomes. The chapter ends with a detailed discussion on findings related to patients' medication adherence and clinical outcomes, direct healthcare costs and satisfaction along with a brief conclusion.

Chapter 7 is the thesis conclusion and also the final chapter of this thesis. This chapter starts with a summary of the study followed by study limitations along with a set of recommendations. The chapter ends by highlighting suitable future research and the conclusion.

CHAPTER 2

LITERATURE REVIEW AND RESEARCH CONCEPTUAL FRAMEWORK

2.1 Definition of Diabetes mellitus

Diabetes mellitus (DM) represents a group of metabolic disorders and is characterized by an increase in blood glucose level termed as 'hyperglycaemia'. It is associated with abnormalities in carbohydrate, fat and protein metabolism that results due to defects in insulin secretion, insulin action or a combination of both. Several pathogenic factors are responsible for abnormality in insulin secretion and insulin action, which range from autoimmune destruction of pancreatic β-cells to abnormalities that result in resistance to insulin action (World Health Organization & International Diabetes Federation, 2006; American Diabetes Association, 2012).

2.2 Classification of diabetes mellitus

Based on the aetiology, most cases of DM falls into two category '*Type 1 diabetes mellitus'* and *'Type 2 diabetes mellitus'*. Apart from this gestational diabetes mellitus (GDM) and diabetes due to drugs (Drug induced diabetes mellitus) and secondary to other disease conditions related with pancreas like acute and chronic pancreatitis etc., are also rarely seen (American Diabetes Association, 2002b).

In case of ***Type 1 DM***, there is absolute deficiency of insulin due to immune-mediated destruction of the pancreatic β-cells. This type of diabetes is common in children and adolescents and can be managed with combination of pharmacological and

non-pharmacological agents like insulin, diet and exercise (Franz et al., 2004). Autoimmune destruction of the β-cells is due to multiple genetic predispositions and environmental factors and are still not well defined (Åkerblom & Knip, 1998; Visalli et al., 2003; Majeed & Mea, 2011). The patients with type 1 diabetes mellitus require exogenous administration of insulin throughout their life for survival (American Diabetes Association, 2012).

Type 2 DM is most common type of diabetes and mainly found in 90-95% of all diabetes cases (American Diabetes Association, 2007). This type of diabetes is also known as *'non insulin dependent diabetes mellitus'* (NIDDM) or *'maturity onset diabetes in youth'* (MODY). Type 2 DM occur due to impaired insulin secretion and insulin resistance of target tissues, mainly liver and skeletal muscles. Type 2 DM patients are in general at an increased risk of developing macro-vascular and micro-vascular complications (Triplitt et al., 2005; American Diabetes Association, 2012). These days large number of people at younger age group is developing type 2 DM due to obesity and sedentary lifestyle (Hu, 2003). It is known that about 80% of type 2 DM are preventable by following a healthy lifestyle, physical activity, maintaining ideal body weight and proper nutritional supplements (International Diabetes Federation, 2009).

Gestational diabetes mellitus (GDM) refers to the detection of glucose intolerance first time during pregnancy. Insulin resistance during pregnancy is mainly due to certain metabolic changes which increases insulin requirement and may lead to hyperglycaemia or impaired glucose tolerance (IGT). Most of the time women revert back to normal glucose tolerance after post-partum with a substantial risk (30-60%) of

developing DM in later phase of the life (Centers for Disease Control and Prevention, 2011).

2.3 Clinical presentation of diabetes mellitus

Type 1 DM individuals are more often thin and prone to develop diabetic ketoacidosis (DKA) due to insulin crisis, or under condition of severe stress with an excess of insulin counter regulatory hormones. About 20-40% of patients with type 1 DM present with diabetic ketoacidosis after several days of polyuria, polydipsia, fatigue, abdominal pain and often with weight loss (Atkinson & Eisenbarth, 2001; Al Magamsi & Habib, 2004; American Diabetes Association, 2007; Razavi, 2010). Commonly, patients of type 2 DM may present with or without diabetes symptoms even though they carry the complications indicating that they have diabetes since several years. Type 2 DM patients may present with lethargy, polyuria, nocturia and polydipsia at diagnosis, and at times associated with weight loss (Triplitt et al., 2005).

2.4 Diagnosis of diabetes mellitus

Normally the diagnosis of diabetes is performed only when the patient shows one or more usual symptoms of diabetes. Early diagnosis can render better management of diabetes and thus delaying the long term complications. The level of blood sugar is measured in venous blood sample. The diagnosis of diabetes is performed on the basis of the criteria given by American Diabetes Association (American Diabetes Association, 2007).